## Remarks

Non-elected Subject Matter

The Final Office Action notes that the pending claims "encompass administering to the mammal a nucleic acid molecule comprising a coding sequence for any of the neuronal marker protein [sic] listed in claims 10 and 11." Final Office Action at page 24 ¶ 1.[1] The Restriction Requirement mailed October 21, 2005 required species elections. Applicants elected the species of retinal cell degeneration and the neuronal marker *M. musculus* retinal S antigen. Applicants have not canceled the non-elected species because Applicants would like the patentability of claims 10-12 and 18 to be considered with respect to the non-elected subject matter once the claims are found allowable. M.P.E.P. § 809.02(e).

The Rejection of Claims 10-12 and 18 Under 35 U.S.C. § 112 ¶ 1

Claims 10-12 and 18 stand rejected under 35 U.S.C. § 112 ¶ 1 as not enabled. Applicants respectfully traverse the rejection.

The claims are directed to methods of reducing neuronal cell death in a mammal. Independent claim 10 recites administering to the mammal a nucleic acid molecule comprising a coding sequence for the neuronal marker *M. musculus* retinal S antigen. Independent claim 11 recites administering to the mammal purified *M. musculus* retinal S antigen. The U.S. Patent and Trademark Office has the initial burden to establish a reasonable basis to question the specification's enablement of the claims. *In re Wright*, 999 F.2d 1557, 1562, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). To make a *prima facie* case of non-enablement using this standard, an Examiner must properly construe the claims and must weigh all the evidence and establish a

[1] This is true with respect to claims 10 and 12; claim 11 recites administering the protein itself.

reasonable basis to question the enablement provided in the specification for the claimed invention. M.P.E.P. §§ 2164.04 and 2164.05, 8th ed., revised August, 2006.

The Examiner has applied the wrong standard to the enablement analysis of this application. The Examiner continues to require the type of disclosure which would be required by the FDA to approve clinical use of the invention. For example, the Final Office Action states, without citing any case law, "It is noted that for a therapy claim to be enabled, there has to be evidence of therapeutic effect . . . the evidence of therapy is required to support enabling disclosure." Final Office Action at page 22 ¶ 3. To the contrary, there is no requirement that an invention be actually reduced to practice, nor are working examples required to enable an invention. *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 U.S.P.Q.2d 1302, 1304 (Fed. Cir. 1987); *In re Long*, 368 F.2d 892, 895, 151 U.S.P.Q. 640, 642 (C.C.P.A. 1966).

The specification is directed to those skilled in the art. With the response filed July 5, 2006 Applicants provided forty-four references which attest to the ability of those skilled in the art in July 2003, when this application was filed, to transfer and express exogenous genes effectively in neurons *in vivo*. Applicants also provided sixteen references which attest to the ability of those skilled in the art to administer proteins effectively to reduce or prevent neuronal death *in vivo* at the time the application was filed. Because it is closer to the filing date of the application, this evidence is far more relevant than the 1995-1999 references on which the Final Office Action relies. The Final Office Action points to only two references (Shah[2] and Thomas[3]) as being "close to the filing date." Final Office Action at page 22 ¶ 1. Neither reference is

[2] Shah *et al.*, *Adv. Genetics 54*, 339-61, 2005.

[3] Thomas *et al.*, *Nature 4*, 346-58, 2003.

probative. Shah describes clinical trials – again, requiring a higher standard than enablement – involving non-viral gene therapy for therapeutic angiogenesis in humans with myocardial ischemia and peripheral vascular disease; these trials are not relevant to the claimed methods of reducing neuronal death. Thomas, although published closer to Applicants' July 2003 filing date, in May 2003, reviews earlier gene therapy research and is therefore no more relevant than the earlier published primary references cited by the PTO.

All the evidence of record must be considered in its entirety. *In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992). When correctly analyzed, the weight of evidence of record in this application favors a finding of enablement of claims 10-12. Applicants respectfully request withdrawal of the rejection.

Respectfully submitted,

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Date: December 19, 2006 By: _____

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